

Application No. 10/584,484  
Amendment dated 3/8/10  
Reply to Office action of 12/7/09

DRAWING AMENDMENTS

The attached sheet of drawings includes changes to Fig. 4. Specifically, reference numerals 32, 33, 34, and 35 have been added.

Please approve the drawing changes that are marked in red on the accompanying "Annotated Sheet Showing Changes". A formal replacement sheet of amended Fig. 4 is also enclosed.

Attachments: Replacement Sheet

Annotated Sheet Showing Changes

REMARKS

Reconsideration of the subject application is respectfully requested.

Claims 1-13 and 17-19 were pending as of the Office Action mailing date of December 7, 2009. This Reply is timely filed within the three (3) month time period for reply set forth in the Action.

As correctly indicated on page 2 of the Office Action, claim 13 has been withdrawn. The current listing of the claims in this Reply has a correct status identifier for claim 13.

Claim 1 has been amended and claim 8 has been cancelled herewith. No new matter is added by any of the claim amendments.

**I. OBJECTION TO THE DRAWINGS**

The Office Action has set forth several objections to the drawings.

Applicant addresses each objection below:

**A. Objection to page 12, line 6**

Applicant has amended the specification to clarify that the array substrate discussed in relation to Fig. 1 is found in Fig. 2. The amendment, beginning on page 11, line 36 now refers to Figs. 1 and 2.

**B. Objection to page 14, line 27**

Applicant has amended the specification to properly identify the diameter as figure element 30.

**C. Objection to page 15, lines 27-34**

Applicant has amended the specification to indicate each of substrate 28, support layer 6, and nanopores 8, are present in Fig. 2.

Replacement sheet for Fig. 4 has figure drawing elements for each of chip 32, PMMA 34, and substrate 35. The specification has been amended to indicate each of these are present in Fig. 4.

Applicant believes all objections to the drawings have been addressed and respectfully requests reconsideration and withdrawal of these objections.

**II. SPECIFICATION**

The Specification has been objected to based on a missing description of Fig. 4.

Applicant has amended the Specification to include a brief description of Fig. 4.

Applicant respectfully requests reconsideration and withdrawal of this objection.

**III. REJECTION OF CLAIMS 1-5, 8-12, AND 17-18 UNDER 35 USC 102(a) OR 102(e).**

Claims 1-5, 8-12, and 17-18 have been rejected under 35 USC 102(a) or 102(e) as anticipated by US patent application publication No. 2003/0104512 to Freeman.

Applicant respectfully traverses this rejection.

The current invention, as now claimed, requires, inter alia:

a biologically effective layer configured to host at least one of a non-lipid molecule and functional molecule, deposited on said support layer and covering the plurality of nanopores, resulting in accessible nanopores from both sides of the biologically effective layer for measurements; wherein the biologically effective layer is a biomembrane isolated from one of prokaryotic and eukaryotic cells, and wherein the biologically effective layer is a lipid bilayer formed by preparation and later fusion of lipid vesicles or is a functional layer of supramolecular assembly (amended claim 1)

The claim, as now presented requires specifically “the biologically effective layer is a biomembrane isolated from one of prokaryotic and eukaryotic cells, and wherein the biologically effective layer is a lipid bilayer formed by preparation and later fusion of lipid vesicles or is a functional layer of supramolecular assembly.”

The cited Freeman reference is deficient for failing to teach the claimed biomembrane or the lipid bilayer.

With respect to the Office Action assertion that Freeman et al. is disclosing a cellular layer 84 that could host a non-lipide molecule and functional molecule, the applicant respectfully traverses this assertion as being physically and functionally completely different from the biologically effective layer that the present invention provides.

The biologically effective layer is a crucial component of the present assay chip because it is the aim of the present invention to study the biological interactions under vital conditions. Therefore, the mechanically stabilized biological effective layer (that means the solid support layer being the  $\text{Si}_3\text{N}_4$ -membrane with the nanopores and the biological effective layer being immobilized thereupon) offers free access from both sides of the biological effective layer what allows the investigation of complex interactions of molecules, such as natural ligands or the interaction with artificial effector molecules (such as drugs) with functional integrated membrane proteins and to elucidate the mechanism of signal transduction.

Due to the accessibility from both sides, the transport of ions, molecules and particles through the biological effective layer by transporter proteins can be investigated in a micro-chamber system, i.e. in a two-compartment system. Surface patterning and microspotting technologies will allow to address specific nanopore arrays. Furthermore, due to the use of the biologically effective layer as now claimed in claim 1, the membrane proteins are sterically not impeded due to the preservation of their mobility and therefore can directly be investigated on their response to allosteric effects what is crucial for the development of new drugs with GCPRs as the target, for example.

**Only** a biologically effective layer that offers vital condition allows an un-impeded diffusion of macromolecules to both, the lipid bilayer membrane and the non-lipid molecule, such as membrane proteins, integrated in the lipid bilayer membrane.

The assay chip of the present invention has the structure and configuration that allows the study under vital conditions.

Freeman is only a study of whether a specific non-lipid molecule allows an ion-transfer. The present invention is a study under which circumstances (e.g. when specific natural ligands couple to the binding sites of the non-lipid molecule) some of the biological interactions may occur. Without being disposed in a vital lipid bilayer membrane, the non-lipid molecule can neither move along the lipid bilayer membrane nor can it send out second messenger molecules that allow other biological molecules to be attached to the lipid bilayer membrane and allow the transfer of different components other than those being allowed to cross the membrane at the site of the first non-lipid molecule.

Summarized, Freeman et al. is lacking the biologically effective layer disposed on the support layer. Therefore, the structure of Freeman et al. is not able to observe biological interactions which can only take place when a non-lipid molecule is implanted into the biologically effective layer offering real vital conditions for non-lipid molecule.

Thus, Freeman is not anticipatory and in fact is contrary to the system of the present invention.

Applicant reminds the Office:

"[A]nticipation under § 102 can be found only when the reference discloses exactly what is claimed and that where there are differences between the reference disclosure and the claim, the rejection must be based on § 103 which takes differences into account." *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

Claim 1 is respectfully asserted not anticipated by the reference because the claim requires, at least, a biologically effective layer disposed on the support layer, as now claimed.

Because of the failure of the Freeman reference to teach each and every element of the claimed invention, Applicant asserts a rejection under 35 USC 102 cannot be properly applied.

Applicant respectfully request reconsideration and withdrawal of this rejection.

#### **IV. REJECTION OF CLAIMS 6, 7, and 19 UNDER 35 USC 103(a)**

Claims 6, 7, and 19 have been rejected under 35 USC 103(a) as being obvious over the aforementioned Freeman reference in view of U.S. patent No. 5,843,767 to Beattie.

Applicant respectfully traverses this rejection.

Claims 6, 7, and 19 are dependent claims depending ultimately on claim 1 and including all the limitations of the base claim.

Applicant recognizes and acknowledges that this rejection is based on the combined teaching of the Freeman and Beattie references.

The Freeman reference is deficient, as set forth above in sec. III of this Reply.

Applicant asserts that sec. III sets forth sufficient distinctions that demonstrate the subject is neither anticipated by, nor obvious, in view of the Freeman reference.

Combination of Freeman with Beattie to a single combined disclosure is still deficient for failing to teach, suggest, or provide motivation to modify in order to arrive at the present invention having the biologically effective layer disposed on the support layer as currently claimed.

Beattie is cited in the Office Action, page 6, as teaching a microfabricated, flow-through, porous apparatus, for detecting binding reactions.

The porous apparatus of Beattie does not teach or suggest the claimed biologically active layer with any amount of disclosure such that, in combination with Freeman, the subject invention encompassed by independent claim 1, and dependent claims 6, 7, and 19 can be rendered obvious.

Because the combined disclosure of Freeman and Beattie remains deficient for providing any teaching, suggestion or motivation to modify in order to arrive at the claimed subject invention, Applicant asserts a rejection under 35 USC 103(a)

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Based upon the amendments and representations presented herein, Applicant respectfully asserts the application is now in condition for allowance. If the Examiner believes there are any issues that have not been resolved the Examiner is invited to call the undersigned representative who is attorney of record in this case.

Please charge any fees that might be due with respect to Sections 1.16 and 1.17 to Deposit Account Number 12-1099 of Lerner Greenberg Stemer LLP.

Respectfully submitted,

/Laurence A. Greenberg/  
Laurence A. Greenberg  
Reg. No. 29308

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Lerner Greenberg Stemer LLP  
P.O. Box 2480  
Hollywood, Florida 33022-2480  
Tel.: (954) 925-1100  
Fax: (954) 925-1101

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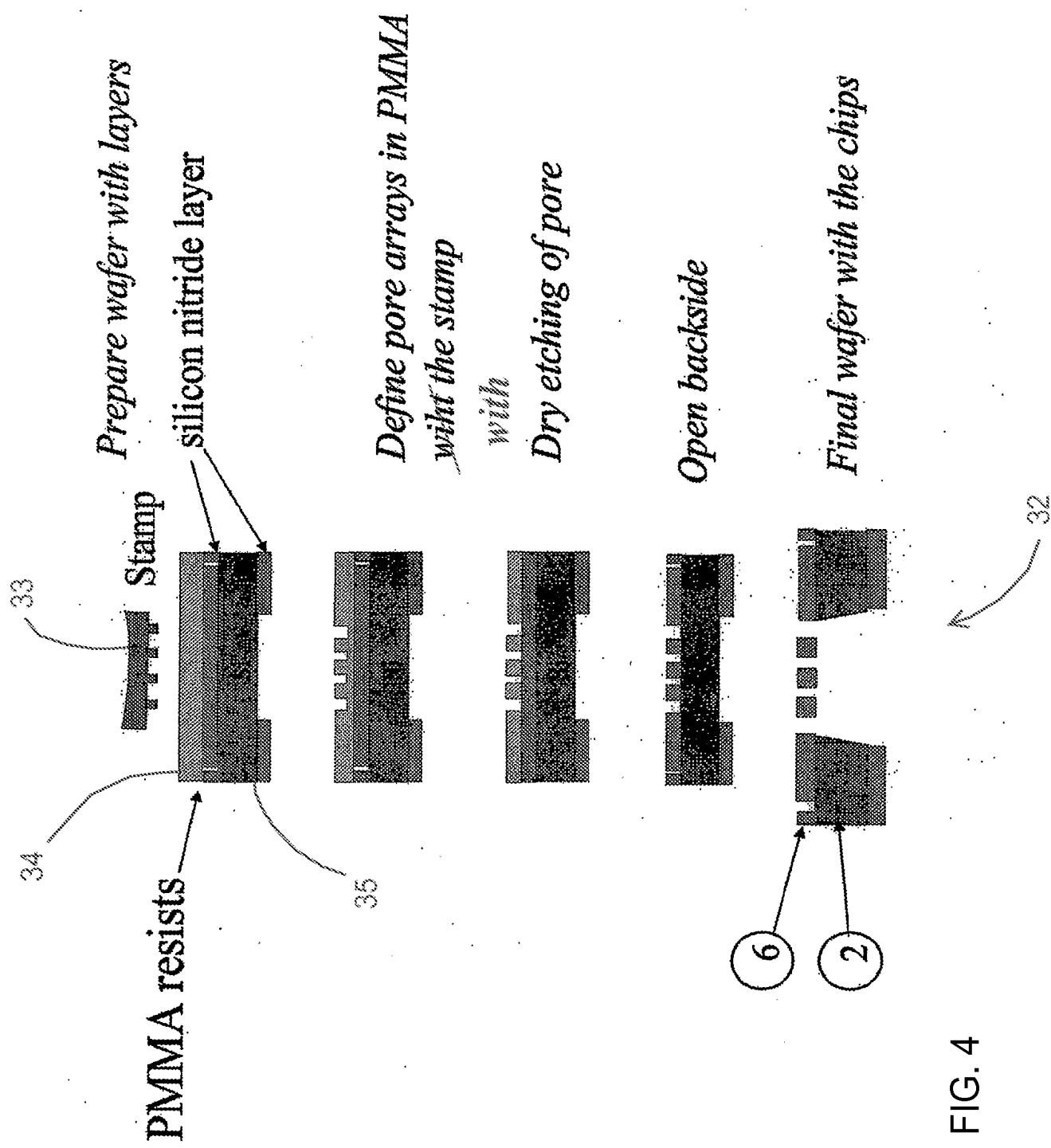


FIG. 4